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Dep & Ref.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

BICHON et al

Atty. Ref.: 1201-83

Serial No. 09/706,778

Group: 1619

Filed: November 7, 2000

Examiner:

For: GAS OR AIR FILLED POLYMERIC MICROBALLOONS

* * * * *

March 9, 2001

Assistant Commissioner for Patents

Washington, DC 20231

Sir:

REQUEST FOR REFUND

Our Deposit Account was charged \$160.00 under code 102 independent claims in excess of three and \$558.00 under code 103 for claims in excess of twenty. When this divisional application was filed claims 3-31 were canceled on the cover sheet (copy attached), claims 1 and 2 canceled in the Preliminary Amendment and new claims 32-50 added. Cancellation of these claims left a total number of claims in the application of 34 with one independent claim. A refund is respectfully requested for the charge to our

Deposit Account for claims over the number of claims in the application. Please credit

our Deposit account no. 14-1140 under Order No. 1201-83 in the amount of \$718.00 for

these erroneous charges. For this purpose a duplicate copy of this paper is enclosed.

Adjustment Date: 04/06/2001 HDENDY
02/08/2001 ABRAHAM 00000021 141140 09706778
01 FC:102
02 FC:103

BICHON et al
Serial No. 09/706,778

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____



Arthur R. Crawford

Reg. No. 25,327

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Telephone: (703) 816-4000
Facsimile: (703) 816-4100

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Division of Patent Application Serial No. 08/910,152 of

BICHON et al

Serial No. to be assigned

Filed: November 7, 2000

For: GAS OR AIR FILLED POLYMERIC MICROBALLOONS



Atty. Ref.: 1201-83

Group:

Examiner:

* * * * *

November 7, 2000

Assistant Commissioner for Patents
Washington, DC 20231

COPY

Sir:

PRELIMINARY AMENDMENT

In order to place the above-identified application in better condition for examination, please amend the application as follows:

IN THE SPECIFICATION

Page 1, after the title insert the following:

--CROSS-REFERENCE TO RELATED APPLICATIONS

This is a division of Serial No. 08/910,152 filed August 13, 1997, now U.S. , which is a division of Serial No. 08/288,550 filed August 10, 1994, now U.S. 5,711,933, which is a division of Serial No. 08/033,435 filed March 18, 1993, abandoned, which is a division of Serial No. 07/695,343 filed May 3, 1991, abandoned.--.

Page 9, lines 7 and 8 delete and insert the following:

--Air or gas filled microballoons of the invention useful as suspensions in a carrier liquid for oral, rectal, or urethral applications, or for injections into living organisms, are prepared by (1) emulsifying a hydrophobic organic phase into a water phase so as to obtain droplets of the hydrophobic phase as an oil-in-water emulsion in the water phase; (2) adding to the emulsion a solution of at least one polymer in a volatile solvent insoluble in the water phase, so that a layer of the polymer will form around the droplets; (3) evaporating the volatile solvent so that the polymer will deposit by interfacial precipitation around the droplets which then form beads with a core of the hydrophobic phase encapsulated by a membrane of the polymer, the beads being suspended in the water phase; then (4) subjecting the suspension to reduced pressure under conditions such that the encapsulated hydrophobic phase is removed by evaporation. The hydrophobic phase is selected so that in step (4) it evaporates substantially simultaneously with the water phase and is replaced by air or gas, whereby dry, free flowing, readily dispersible microballoons are obtained. Alternatively, the polymer is dissolved in the hydrophobic phase, so that steps (2) and (3) can be omitted and the polymer membrane will form by interfacial precipitation during step (4).--.

Page 8, line 11, delete "of the"

lines 12 and 13, delete entirely and insert:

-- , e.g. under conditions for freeze drying. For instance, --

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IN THE CLAIMS

Cancel claims 1 and 2 and add the following new claims:

--32. Dry microballoons which, upon dispersion in an aqueous carrier liquid, form an aqueous dispersion comprising microballoons bounded by a 50-500 nm thick polymer membrane filled with air or a gas, the microballoons having a mean size in the range of a fraction of micron to 1000 microns and the membrane polymer being biodegradable, synthetic, deformable, resilient and selected from the group of interfacially depositable polymers.

33. The dry microballoons of claim 32, wherein the microballoons have size in the range of 0.5-10 μm and the membrane is either impervious or permeable to bioactive liquids for increasing the rate of biodegradation.

34. The dry microballoons of claim 32, wherein the polymer membrane is porous and has porosity ranging from a few nanometers to several thousands of nanometers.

35. The dry microballoons of claim 34, wherein the polymer membrane has a porosity of 50 to 2,000 nm.

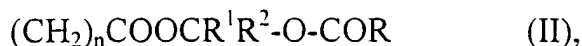
36. The dry microballoons of claim 32 or 33 wherein the polymer of the membrane is a biodegradable polymer selected from the group consisting of polysaccharides, polyamino-acids, polylactides and polyglycolides and their copolymers, copolymers of lactides and lactones, polypeptides, poly-(ortho)esters, polydioxanone, poly- β -aminoketones, polyphosphazenes, polyanhydrides and polyalkyl-(cyano)acrylates.

37. The dry microballoons of claim 32 or 33 wherein the membrane polymer is selected from the group consisting of polyglutamic or polyaspartic acid derivatives and their copolymers with other amino acids.

38. The dry microballoons of claim 37, wherein the polyglutamic and polyaspartic acid derivatives are selected from the group consisting of esters and amides involving a carboxylated side function, said side function having formulae:



or



or



where R is an alkyl or aryl substituent; R^1 and R^2 are H or lower alkyls, or R and R^1 are connected together by a substituted or unsubstituted linking member to form a 5- or 6-membered ring; n is 1 or 2; p is 1, 2 or 3; m is an integer from 1 to 5 and X is a side chain of an amino acid residue.

39. The dry microballoons of claim 32 or 33, wherein the membrane polymer contains additives to control the degree of elasticity and the size and density of the pores for permeability control.

40. The dry microballoons of claim 39, wherein said additives include plasticizers, amphipatic substances and hydrophobic compounds.

41. The dry microballoons of claim 40, wherein the plasticizers include isopropyl myristate, glyceryl monostearate and the like to control flexibility, the amphipatic

substances include surfactants and phospholipids like the lecithins to control permeability by increasing porosity and the hydrophobic compounds are high molecular weight hydrocarbon paraffin-waxes to reduce porosity.

42. The dry microballoons of claim 40, wherein the additives include polymers of molecular weight in the range of 1000 to 15,000 to control softness and resiliency of the microballoon membrane.

43. The dry microballoons of claim 42, wherein the polymer additives are selected from the group consisting of polylactides, polyglycolides, polyalkylene glycols like polyethylene glycol and polypropylene glycol, and polyols.

44. The dry microballoons according to claim 32 or 33, wherein the gas in the microballoons is a freon.

45. The dry microballoons according to claim 32 or 33, wherein the gas in the microballoons is N_2O ,

46. The dry microballoons according to claim 32 or 33, wherein the gas in the microballoons is a rare gas.

47. The dry microballoons according to claim 32 or 33, wherein the gas in the microballoons is methane.

48. The dry microballoons according to claim 32 or 33, wherein the gas in the microballoons is helium.

49. The dry microballoons according to claim 32 or 33, wherein the gas in the microballoons is CO_2 .

50. The dry microballoons according to claim 32 or 33, wherein the gas in the microballoons is a radioactive tracer gas.

REMARKS

This application is a division of earlier application Serial No. 08/910,152 which was allowed on September 25, 2000.

The claims in this application are directed to dry microballoons.

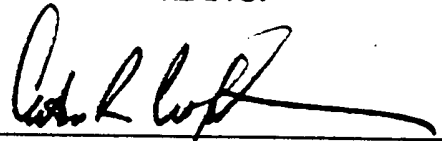
The specification has been amended consistent with the amendments made to the prior application and attached please find an Information Disclosure Statement citing the art of record in the parent application. Copies of this art are available in the prior application.

An examination on the merits is awaited.

Respectfully submitted,

NIXON & VANDERHYE P.C.

By: _____



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Reg. No. 25,327

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
REQUEST FOR FILING APPLICATION UNDER RULE 1.53(b)**

Pursuant to 37 CFR 1.53(b), please file a ☐ continuation/☒ divisional
of the pending prior PATENT APPLICATION of:

Inventor: BICHON et al

Serial No. 08/910,152

Filed: August 13, 1997

Title: **GAS OR AIR FILLED POLYMERIC MICROBALLOONS**

Assistant Commissioner for Patents

Washington, DC 20231

Sir:

This request for filing under Rule 53(b) is made by the following named inventor(s) (using the above-identified title):
Inventor(s): BICHON et al

- ☒ Attached is a true copy of the prior application as originally filed including the specification, claims, Oath/Declaration and drawings (if any) and abstract (if any). No amendments (if any) referenced in the Oath or Declaration filed to complete the prior application introduced new matter.
- ☒ Priority is hereby claimed under 35 USC 119 based on the following foreign applications, the entire content of which is hereby incorporated by reference in this application:

Application Number

90810367.4

Country

EP

Day/Month/Year/Filed

18 May 1990

☐ certified copy(ies) of foreign application(s) attached or

☒ already filed on May 3, 1991 in prior appln. no. 07/695,343 filed May 3, 1991

☐ already filed in filed

- ☒ The prior application is assigned to Bracco International B.V..
- ☒ Power of Attorney has been granted to Arthur R. Crawford et al, Reg. No. 25,327 of Nixon & Vanderhye P.C., 1100 N. Glebe Rd., 8th Floor, Arlington, VA 22201.
- ☒ Address all future communications to: Nixon & Vanderhye P.C., 1100 N. Glebe Rd., 8th Floor, Arlington, VA 22201.
- ☒ Please amend the specification by inserting before the first line --This is a division of application Serial No. 8/910,152, filed August 13, 1997, now U.S. patent _____, which is a division of Serial No. 08/288,550 filed August 10, 1994, now U.S. 5,711,933, which is a division of Serial No. 08/033,435 filed March 18, 1993, abandoned, which is a division of Serial No. 07/695,343 filed May 3, 1991, abandoned-- the entire content of which is hereby incorporated by reference in this application.--
- ☒ The Examiner's attention is directed to the prior art cited in the parent application by applicant and/or Examiner for the reasons stated therein.
- ☒ Please enter the attached and/or below preliminary amendment **prior** to calculation of filing fee:
Claims 3-31.
- ☒ The entire disclosure of the prior application above-referenced is considered as being part of the disclosure of this new application and is hereby incorporated by reference therein.

FILING FEE IS BASED ON CLAIMS AS FILED LESS ANY HERewith CANCELED

Basic Filing Fee			\$	710.00
Total effective claims	34	- 20 (at least 20) =	14 x \$ 18.00	\$ 252.00
Independent claims	1	- 3 (at least 3) =	0 x \$ 80.00	\$ 0.00
If any proper multiple dependent claims now added for first time, add \$270.00 (ignore improper)				\$ 270.00
SUBTOTAL				\$ 1232.00
If "small entity," then enter half (1/2) of subtotal and subtract				\$(0.00)
SECOND SUBTOTAL				\$ 1232.00
Assignment Recording Fee (\$40.00)				\$ 0.00
TOTAL FEE ENCLOSED				\$ 1,232.00

Any future submission requiring an extension of time is hereby stated to include a petition for such time extension. The Commissioner is hereby authorized to charge any deficiency in the fee(s) filed, or asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our **Account No. 14-1140**. A duplicate copy of this sheet is attached.

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NIXON & VANDERHYE P.C.
By Atty: Arthur R. Crawford, Reg. No. 25,327

Signature: _____

Arthur R. Crawford

COPY



Atty Dkt.: 1201-83
C# M#
Date: November 7, 2000
Group: 1616
Examiner: Hollinden